Metal Ion-Complexes of α,β-Unsaturated Ketones Acting as Actual Reactive Species in Michael Addition of Ketene Silyl Acetal

Shunichi Fukuzumi,* Toshihiko Okamoto, Kiyomi Yasui, Tomoyoshi Suenobu, Shinobu Itoh, and Junzo Otera*†
Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565
†*Department of Applied Chemistry, Okayama University of Science, Ridai-cho, Okayama 700*

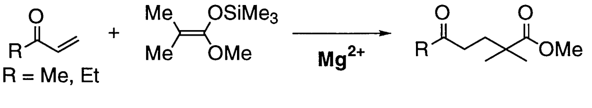
(Received April 7, 1997; CL-970252)

The Michael addition of β,β-dimethyl-substituted ketene silyl acetal [$Me_2C=C(OMe)OSiMe_3$] with α,β-unsaturated ketones occurs efficiently in the presence of magnesium perchlorate or lutetium trifluoromethanesulfonate in acetonitrile at 298 K via the 1 : 1 complexes between α,β-unsaturated ketones and the metal ion, in which the coordination of the metal ion enhances the electrophilicity of α,β-unsaturated ketones to accelerate the reaction rate.

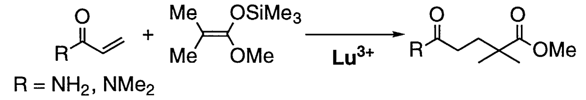
Lewis acid-promoted Michael addition of ketene silyl acetals to α-enones (Mukaiyama-Michael reaction) has been a powerful means for carbon-carbon bond formation.[1,2] Strong Lewis acids such as $TiCl_4$ and $SnCl_4$ are usually required for these transformations. Lanthanide trifluoromethanesulfonates also work well in the Mukaiyama-Michael reaction as well as in the other C-C bond formation reactions, i.e. Aldol reactions, Diels-Alder reactions, Friedel-Crafts acylations and so on.[3] Very high concentrations of lithium perchlorate which is regarded as a mild Lewis acid in diethyl ether have also been reported to be effective to promote the Michael addition as well as the Diels-Alder reaction.[4,5] We have also reported that $Mg(ClO_4)_2$ acts as an efficient catalyst for the nucleophilic addition of ketene silyl acetals as well as the Diels-Alder reaction of anthracenes with quinones in MeCN.[6,7] In each case coordination of Lewis acid to carbonyl oxygen is believed to enhance the electrophilicity, resulting in the efficient nucleophilic attack of ketene silyl acetals.[1-7] However, no kinetic study on the Lewis acid-promoted Michael addition has so far been reported to elucidate the actual role of Lewis acid in the reaction.

This study reports that the Michael addition of β,β-dimethyl-substituted ketene silyl acetal [$Me_2C=C(OMe)OSiMe_3$] with α,β-unsaturated ketones, $H_2C=C(H)COR$ (R = Me, Et, NH_2 and NMe_2) occurs efficiently in the presence of magnesium perchlorate [$Mg(ClO_4)_2$] and lutetium trifluoromethanesulfonate [$Lu(OTf)_3$] in acetonitrile (MeCN) at 298 K. The present system is suitable to the kinetic analysis, since the time course can be readily monitored by the change in the electronic spectra. Thus the present study provides an excellent opportunity to elucidate the actual role of the mild Lewis acid complex in the Michael addition for the first time.

No reaction occurs between β,β-dimethyl-substituted ketene silyl acetal [$Me_2C=C(OMe)OSiMe_3$] and α-enones in MeCN at 298 K.[8] When $Mg(ClO_4)_2$ is added to the acetal-enone system, however, the Michael addition of $Me_2C=C(OMe)OSiMe_3$ with vinyl ketones ($H_2C=C(H)COR$, R = Me, Et) occurs efficiently at 298 K to yield the adduct as shown in Equation 1.[9] When the vinyl ketone is replaced by (*E*)-$MeC(H)=C(H)COEt$ and $Me_2C=C(H)$-COMe, however, no reaction occurs under otherwise the same experimental conditions, indicating the significant steric effect of methyl group of the enones. Acrylamide and *N*,*N*-dimethylacrylamide also show no reactivity. When $Lu(OTf)_3$ is used as a catalyst instead of $Mg(ClO_4)_2$, however, the Michael addition of $Me_2C=C(OMe)OSiMe_3$ with $H_2C=C(H)CONH_2$ and $H_2C=C(H)CONMe_2$ occurs efficiently to yield the corresponding adducts (Equation 2).[9]



(1)



(2)

The rates of Mg^{2+}- and Lu^{3+}-catalyzed Michael addition of $Me_2C=C(OMe)OSiMe_3$ with α-enones were followed by the disappearance of the absorbance (λ = 350 nm) due to α-enones. The rates with the large excess acetal obeyed strictly the pseudo-first-order kinetics. The pseudo-first-order rate constants are proportional to the acetal concentrations. Thus, the rate shows a first-order dependence on each reactant. The observed second-order rate constant (k_{obs}) increases linearly with an increase in the metal ion concentration [M^{n+}] ($M^{n+} = Mg^{2+}$ and Lu^{3+}) at low concentration and reaches the limiting value at high concentration as shown in Figure 1 in the case of Lu^{3+} as a catalyst. Such a saturated dependence of k_{obs} on [M^{n+}] may be explained by the formation of 1 : 1 complex of M^{n+} and the enone, which may act as a strong electrophile as compared with free enone in the Michael addition as shown in Scheme 1.

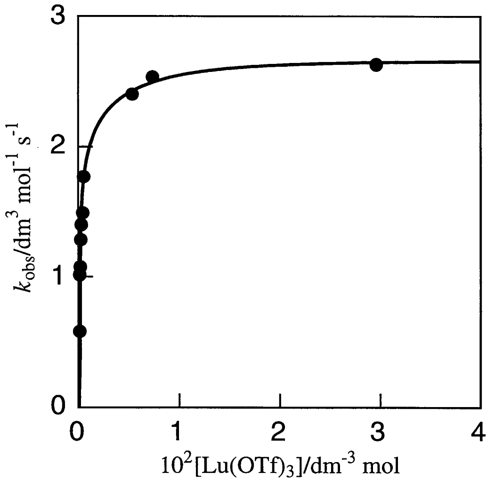


Figure 1. Dependence of k_{obs} on [$Lu(OTf)_3$] for the Michael addition of $Me_2C=C(OMe)OSiMe_3$ (2.0×10^{-3} dm^{-3} mol) with *N*,*N*-dimethylacrylamide (1.0×10^{-4} dm^{-3} mol) in deaerated MeCN at 298 K.

Table 1. Rate constants (k) of Mg^{2+}- and Lu^{3+}-catalyzed Michael addition of $Me_2C{=}C(OMe)OSiMe_3$ with α-enones ($H_2C{=}C(H)COR$) and the formation constants (K) of the metal ion complexes of α-enones in MeCN at 298 K

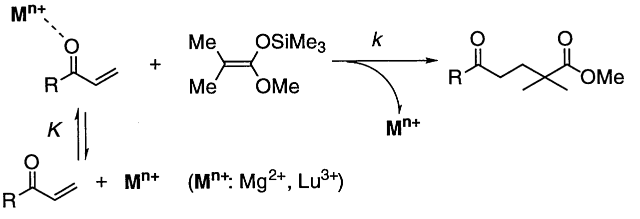
R	Metal ion	k [a] /dm^3 mol^{-1} s^{-1}	K [a] /dm^3 mol^{-1}	K [b] /dm^3 mol^{-1}
Me	Mg^{2+}	0.14	0.60	0.59
Et	Mg^{2+}	0.12	0.33	0.28
NH_2	Lu^{3+}	3.0	1.5×10^3	1.8×10^3
NMe_2	Lu^{3+}	2.5	5.5×10^3	6.1×10^3

[a] Determined from the dependence of k_{obs} on $[M^{n+}]$ according to Equation 3. [b] Determined from Benesi-Hildebrand plots for the change of absorption spectra of α-enones in the presence of metal ion.

According to Scheme 1, the dependence of observed second-order rate constant on $[M^{n+}]$ is expressed by Equation 3. The

$$k_{obs} = kK[M^{n+}]/(1 + K[M^{n+}]) \qquad (3)$$

validity of Equation 3 is confirmed by a linear plot of k_{obs}^{-1} *vs.* $[M^{n+}]^{-1}$. From the slopes and intercepts are obtained the formation constants K for the M^{n+} complexes with α-enones and the rate constants k of the Michael addition of the ketene silyl acetal with the M^{n+} complexes as listed in Table 1.



Scheme 1.

The complexation of α-enones with M^{n+} is studied from the electronic spectral change of α-enones in the presence of M^{n+} in MeCN at 298 K. The π-π* band of ethyl vinyl ketone (λ_{max} = 208 nm) is red-shifted in the presence of $Mg(ClO_4)_2$ (λ_{max} = 220 nm), while the n-π* band (λ_{max} = 322 nm) is blue-shifted to 296 nm. Such spectral change can be explained by the formation of 1:1 complexes between Mg^{2+} and α-enones. The formation constants K are obtained from the Benesi-Hildebrand plots,[10] where $(A - A_0)^{-1}$ are plotted against $[Mg(ClO_4)_2]^{-1}$; A and A_0 are absorbances due to the Mg^{2+} complexes of α-enones and free α-enones, respectively. Similarly the formation constants K for the Lu^{3+} complexes of the amides are determined from the spectral change in the presence of various concentrations of $Lu(OTf)_3$. The K values in MeCN at 298 K thus determined are also listed in Table 1 and they agree with those determined independently from the dependence of k_{obs} on $[M^{n+}]$ for the M^{n+}-catalyzed Michael addition. Such an agreement has provided the first kinetic evidence to show the actual catalytic role of Lewis acid complexes as shown in Scheme 1, where the M^{n+} complexes of α-enones act as reactive electrophiles toward nucleophilic attack of the ketene silyl acetal.

The ^{13}C NMR signals of β-carbon and carbonyl carbon of methyl vinyl ketone exhibit large downfield shifts in the presence of $Mg(ClO_4)_2$ as compared with those in the absence of $Mg(ClO_4)_2$, demonstrating the development of positive charge by the complexation with Mg^{2+} to increase the electrophilicity of β-carbon of the α-enone.

This work was supported by a Grant-in-Aid for Scientific Research on Priority Areas "New Development of Rare Earth Complexes" Nos. 07230257 and 08220242 from The Ministry of Education, Science, Sports, and Culture.

References and Notes

1 K. Saigo, M. Osaki, and T. Mukaiyama, *Chem. Lett.*, **1976**, 163; C. Gennari, in "Selectivities in Lewis Acid Promoted Reactions", ed by D. Schinzer, Kluwer Academic Publishers, Dordrecht (1989), p. 53.
2 J. Otera, Y. Fujita, N. Sakuta, M. Fujita, and S. Fukuzumi, *J. Org. Chem.*, **61**, 2951 (1996).
3 S. Kobayashi, *Synthesis*, **1994**, 689; S. Kobayashi, I. Hachiya, T. Takahori, M. Araki, and H. Ishitani, *Tetrahedron Lett.*, **33**, 6815 (1992); S. Kobayashi, I. Hachiya, H. Ishitani, and M. Araki, *Synlett*, **1993**, 472; S. Kobayashi and M. Horibe, *J. Am. Chem. Soc.*, **116**, 9805 (1994); S. Kobayashi and I. Hachiya, *J. Org. Chem.*, **59**, 3590 (1994); S. Kobayashi, M. Araki, and I. Hachiya, *J. Org. Chem.*, **59**, 3758 (1994); A. Kawada, S. Mitamura, and S. Kobayashi, *Chem. Commun.*, **1996**, 183.
4 P. A. Grieco, J. J. Nunes, and M. D. Gaul, *J. Am. Chem. Soc.*, **112**, 4595 (1990); H. Waldmann, *Angew. Chem., Int. Ed. Engl.*, **30**, 1991 (1991); M. A. Forman and W. P. Dailey, *J. Am. Chem. Soc.*, **113**, 2761 (1991); J. Ipaktschi and A. Heydari, *Angew. Chem., Int. Ed. Engl.*, **31**, 313 (1992).
5 P. A. Grieco, J. L. Collins, and K. J. Henry, Jr., *Tetrahedron Lett.*, **33**, 4735 (1992); P. A. Grieco, R. J. Cooke, K. J. Henry, and J. M. VanderRoest, *Tetrahedron Lett.*, **32**, 4665 (1991); M. T. Reetz, B. Raguse, C. F. Marth, H. M. Hügel, T. Bach, and D. N. A. Fox, *Tetrahedron*, **48**, 5731 (1992); M. T. Reetz and D. N. A. Fox, *Tetrahedron Lett.*, **34**, 1119 (1993).
6 M. Fujita, S. Fukuzumi, G. Matsubayashi, and J. Otera, *Bull. Chem. Soc. Jpn.*, **69**, 1107 (1996).
7 S. Fukuzumi and T. Okamoto, *J. Am. Chem. Soc.*, **115**, 11600 (1993).
8 V. Berl, G. Helmchen, and S. Preston, *Tetrahedron Lett.*, **35**, 233 (1994).
9 The quantitative formation of the adducts was confirmed by comparing the ^1H NMR spectra with those in the literature, see: T. Hatsui, C. Nojima, and H. Takeshita, *Bull. Chem. Soc. Jpn.*, **62**, 2932 (1989); P. R. Jenkins, K. A. Menear, P. Barraclough, and M. S. Nobbs, *J. Chem. Soc., Chem. Commun.*, **1984**, 1423.
10 H. A. Benesi and J. H. Hildebrand, *J. Am. Chem. Soc.*, **71**, 2703 (1949).